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SUBSTITUTE SPECIFICATION

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ARTIFICIAL ANTIBODY POLYPEPTIDES

5 This application is a divisional of U.S. Serial No. 09/096,749, filed June 12, 1998, which claims priority under 35 U.S.C. 119(e) to provisional application U.S. Serial No. 60/049,410, filed June 12, 1997. These applications are incorporated herein by reference.

10 FIELD OF THE INVENTION

 The present invention relates generally to the field of the production and selection of binding and catalytic polypeptides by the methods of molecular biology, using both combinatorial chemistry and recombinant DNA. The invention specifically relates to the generation of both nucleic acid and polypeptide libraries
15 derived therefrom encoding the molecular scaffolding of Fibronectin Type III (Fn3) modified in one or more of its loop regions. The invention also relates to the "artificial mini-antibodies" or "monobodies," i.e., the polypeptides comprising an Fn3 scaffold onto which loop regions capable of binding to a variety of different molecular structures (such as antibody binding sites) have been grafted.

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BACKGROUND OF THE INVENTION

Antibody structure

 A standard antibody (Ab) is a tetrameric structure consisting of two identical immunoglobulin (Ig) heavy chains and two identical light chains. The heavy and
25 light chains of an Ab consist of different domains. Each light chain has one variable domain (VL) and one constant domain (CL), while each heavy chain has one variable domain (VH) and three or four constant domains (CH) (Alzari et al., 1988). Each domain, consisting of ~ 110 amino acid residues, is folded into a characteristic β -sandwich structure formed from two β -sheets packed against each other, the
30 immunoglobulin fold. The VH and VL domains each have three complementarity